Effectiveness of PET Scan in Postoperative Long Term Follow up of Patients with Nonsmall Cell Lung Cancer

Küçük Hücreli Dişi Akciğer Kanserinde Postoperatif Uzun Dönem Takipte PET Görüntülemenin Etkinliği

Küçük Hücreli Dişi Akciğer Kanserinde PET Görüntüleme / PET Scan in Nonsmall Cell Lung Cancer

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Özet

Amaç: Akciğer kanseri nedeniyle opere edilen hastaların uzun dönem takiplerinde pozitron emisyon tomografisi (PET) kullanımı hakkında oldukça az bilgi vardır. Amacımız, küçük hücreli dışı akciğer kanseri (KHDAK) nedeniyle opere edilen asemptomatik hastaların uzun dönem takiplerinde uzak metastazların saptanmasında PET görünütlemenin etkinliğini saptamaktır.Gereç ve Yöntem: PET görüntüleme altmışbeş asemptomatik hastaya uygulandı. PET görünütüleme sonucu metastaz olarak pozitif gelen hastalara metastazı araştırmak amacıyla MRI ve/veya biopsi yapıldı. Bulgular: Hastaların ortalama yaşı 58.09 ± 8.64 [44-82] yıl ve 57 [87.7 %]'si erkekti. Kırksekiz [73.8%] hastada epidermoid karsinom,15 [23.1%]'inde adeno ve 2 [%3.1]'sinde büyük hücreli karsinom vardı. Postoperatif evreleme 1 [1.5%] hastada evre 1A, 14 [21.5%] 'ünde evre 1B, 1 [1.5%] 'inde evre 2A, 27 [41.5%] 'sinde evre 2B and 22 [33.8%] 'sinde evre 3A şeklindeydi. PET görünütleme ile 7 [10.8%] hastada metastaz saptandı. Bir hastada PET görünütlemenin yanlış pozitif olduğu saptandı. Metastaz bölgeleri 3 [4.5%] hastada akciğer, 3 [4.6%] hastada vertebra ve1 [1.5%] hastada tibiaydı. PET'in uzak metastaz saptamadaki etkinliği %98 olarak hesaplandı, sensitivite %100 ve spesifite %98'di. Sonuç: KHDAK'li asemptomatik hastalarda, postoperatif uzun dönem takipte şühelenilmeyen sistemik hastalığı dışlamada PET görüntüleme konvansiyonel görüntüleme yöntemlerine karşı kullanışlı bir alternatif olabilir.

Anahtar Kelimeler

Uzak Metastaz; PET Görüntüleme; Akciğer Kanseri

Abstract

Aim: There is very few data about the use of positron emission tomography [PET] in the long term follow up of patients operated for lung cancer. We aimed to evaluate the effectiveness of PET scan in detecting distant metastases in the long term follow up of asymptomatic patients operated for non-small cell lung cancer [NSCLC]. Material and Method: PET scan was performed to sixty five asymptomatic patients. The patients who had a positive PET scan for metastasis underwent MRI and/or biopsy to verify metastasis. Result: : Mean age of the patients was 58.09 ± 8.64 [44-82] years, and 57 [87.7 %] of them were male. Forty eight [73.8%] of the patients had epidermoid cell, 15 [23.1%] had adeno and 2 [%3.1] had large cell carcinoma. Postoperative stage of 1 [1.5%] patient was 1A, 14 [21.5%] of them were stage 1B, 1 [1.5%] of them was stage 2A, 27 [41.5%] of them were stage 2B and 22 [33.8%] of them were stage 3A. PET scan detected metastasis in 7 [10.8%] patients. In one patient PET scan was proven to be false positive. Sites of metastases in PET scan were lung in 3 [4.5%] patients, vertebra in 3 [4.6%] patients and tibia in 1 [1.5%] patient. In detecting distant metastases accuracy rate of PET was calculated as 98%, sensitivity was 100%, and specificity was 98%. Discussion: In asymptomatic patients with NSCLC, PET imaging appears to be useful as an alternative to conventional imaging to rule out unsuspected systemic disease in the postoperative long term follow up.

Keywords

Distant Metastasis; PET Scan; Lung Cancer

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Introduction

In patients with non-small cell lung cancer [NSCLC], early detection of distant metastases or local recurrence that can develop in long term after surgery is as important as complete resection of the tumor. The prevalence of recurrence or distant metastases in NSCLC within 2 years after complete resection was reported to be 17.0% - 35.8% [1,2]. Early detection of metastases that can develop postoperatively is an important factor that determines treatment and quality of life.

In the postoperative follow up, complaints and laboratory findings of the patient determine the conventional radiological methods to be used. Positron emission tomography [PET] provides better results than conventional imaging methods in detecting recurrences and distant metastases [3].

PET detected distant metastasis in 15% of the patients in whom conventional staging methods reported absence of distant metastasis [4,5,6]. Most of these patients were symptomatic.

PET can differentiate postoperative scar tissue from residual tumor or recurrence [7]. However, to increase the accuracy of the results, PET is suggested to be performed at least 2 months after surgery and 4-6 months after radiotherapy [8,9].

In this study, we aimed to evaluate the frequency of metastasis in long term follow up of asymptomatic patients who underwent complete resection for NSCLC and to determine the effectiveness of PET scan in detecting these distant metastases.

Material and Method

In the follow up control of patients who underwent surgery for NSCLC, patients were questioned for their complaints and were physically examined. Chest X-ray, complete blood count and blood biochemistry parameters were obtained. PET scan was performed to 65 patients who had no complaints, no pathological finding in physical examination and whose laboratory tests were normal. The patients that had symptoms like hemoptysis, lumbalgia etc. were not admitted to the study and the other methods like CT or MR were performed. Only asymptomatic patients were admitted to the study for the evaluation of distant metastasis. Patients were randomly selected. All shootings were done with the same PET-CT device [Siemens biograf LSO HI-REZ entegre PET-CT]. Suvmax values over 2,5 were received malign. Preoperative PET-CT scans were performed all of the patients after 2003, but before 2003 the other methods like CT and MRI were performed to detect the distance metastasis, and all of the patients were free of metastasis. Patients who had shorter postoperative follow up than 3 months, were not included in the study. Magnetic resonance imaging [MRI] and/or biopsy was performed to the patients whose PET scan result was positive for metastasis to verify the result. Brain MRI was also performed to the patients whose PET scan was positive to evaluate presence of co-existing brain metastasis.

Results

Mean age of the patients was 58.09 ±8.64 [44-82] years and 57 [87,7%] of them were male. Postoperative mean follow up time was 28.7 months [min-max: 3-120 months]. Ten of the patients were 3th month, 10 were 6th month, 16 were 12th month, 11 were 24th month, 12 were 60th month and 1 were 120th months of follow up. The cell type of the tumor was epidermoid carcinoma in 48 [73.8%], adenocarcinoma in 15 [23.1%] and large cell carcinoma in 2 [3.1%] patients. Postoperative stage of the cancer was stage IA in 1 [1.5%], stage IB in 14 [21.5%], stage IIA in 1 [1.5%], stage IIB in 27 [41.5%] and stage IIIA in 22 [33.8%] patients [Table 1]. Tumor was located in the right lung in 30 [46.2%] patients and in the left lung in 35 [53.8%] patients. The type of the lung resection was upper lobectomy in 25 [38.5%], pneumonectomy in 15 [23.1%], inferior lobectomy in 12 [18.5%], superior bilobectomy in 5 [7.7%], inferior bilobectomy in 5 [7.7%] and sleeve lobectomy in 3 [4.6%] patients [Table 1]. Eight [12.3%] patients received adjuvant therapy.

Table 1. Features of the patients in which distant metastasis was detected by PET scan

	Epidermoid (n=48)	Adeno (n=15)	Large Cell (n=2)	Total n (%)
IA	-	1	-	1 (1,5%)
IB	6	7	1	14 (21,5%)
IIA	1	-	-	1 (1,5%)
IIB	22	4	1	27 (41,5%)
IIIA	19	3	-	22 (33,8%)
Total (%)	48 (73,8%)	15 (23,1%)	2 (3,1%)	65

PET scan detected metastasis in 7 [10.8%] patients, preoperative PET scans were normal. The earliest metastasis was detected in the 3th month. Locations of the metastases were lung in 3 [4.6%], vertebrae in 3 [4.6%] patients and tibia in 1 [1.5%] patient. Lung metastases were defined as local recurrence in 2 patients. Postoperative detection times of lung metastases were 3th, 12th and 24nd months, respectively. Histopathological diagnosis was obtained by transthoracic fine needle aspiration as adenocarcinoma, the patients were reoperated, frozen sections were studied for surgical margins, 2 of them were positive and sleeve resection was applied them. The patient with tibia metastasis was at 7th month postoperatively. MRI of the tibia was also reported as metastasis. Histopathological diagnosis was obtained by bone biopsy as epidermoid carcinoma. MRI was performed to the 3 patients who were reported to have vertebrae metastasis by PET scan. MRI verified the positivity in 2 patients. In 1 patient, MRI was reported to be negative for metastasis. In this patient, PET result was proved to be false positive by MRI and 3 months MRI follow up. Patients who were verified to have vertebrae metastases were at 7th and 8th months postoperatively. Brain MRI results were negative in patients with positive PET scan results for metastasis.

Table 2. Stages and cell types of the patients

	PET scan pozitive (n=7)
Cell Type	
Epidermoid	4
Adeno	3
Resection type	
Upper Lobectomy	4
Inferior Bilobectomy	2
Pneumonectomy	1
Stage	
IB	2
IIB	3
IIIA	2
Site of Metastasis	
Lung	3
Vertebrae	3*
Tibia	1
Received Adjuvant Therapy	
Yes	2
No	5

* False positive in 1 patient.

The cell types of the tumors in the patients who had positive PET scan results were epidermoid carcinoma in 4 and adenocarcinoma in 3 patients. Postoperative stages of them were IB in 2, IIB in 3

and IIIA in 2 patients [Table 2].

Prevalence of distant metastasis in long term follow up of asymptomatic NSCLC patients with normal laboratory tests was found to be 9.2% [n=6]. PET was found to be false positive in 1 [1.5%] patient. PET scan has an accuracy rate of 98%, sensitivity of 100%, specificity of 98%, positive predictive value of 85% and negative predictive value of 100% in detecting distant metastasis in the postoperative long term follow up of asymptomatic NSCLC patients.

Discussion

In the long term follow up after surgery, distant metastases and local recurrences can be seen in some patients with NSCLC. Appropriate patient follow up should include a clinical evaluation by a physician who is experienced in the signs and symptoms of distant metastases as well as imaging for distant metastases in subgroups of patients despite the absence of symptoms.

Signs and symptoms of systemic metastases [e.g., fatigue, weight loss, poor appetite, neurological signs and symptoms, bone pain] must be verified, because such a positive clinical evaluation carries a substantial false-positive [FP] rate [10, 11]. Generally, this has been accomplished by a series of imaging tests such as a brain CT or MRI, a bone scan, and an abdominal CT. Imaging modalities are powerful tools for malignant bone involvement and Liu et al reported that FDG PET was found to be the best modality to detect bone metastasis in patients with lung cancer, but MRI had the highest specificity on a per-lesion basis [12]. In some instances, however, a simple test such as a plain skeletal radiograph of a symptomatic area is definitive enough. However, there is a group of patients who have no symptoms or signs of disease in long term follow up but have distant metastases. In patients with NSCLC and a negative clinical evaluation for the presence of distant metastases, there is controversy about the need to confirm this with additional tests. Most medical and radiation oncologists believe that such confirmation is required, whereas most surgeons do not. A more detailed look at the false-negative [FN] rate of the clinical evaluation suggests an explanation for the discrepancy in these viewpoints. In our study, we evaluated the frequency of metastasis in asymptomatic patients and the accuracy rate, sensitivity and specificity of PET scan in detecting these metastases [10].

Yoshino et al [2] reported the rate of recurrence and/or distant metastasis within 2 years after complete resection of NSCLC as 17.0% [39/229] in stage I, 32.2% [19/59] in stage II, 35.8% [54/151] in stage IIIA, and 20.7% [6/29] in stage IIIB. Ohta et al [1] reported this rate as 22% for all stages. In these studies, patients were not differentiated for being symptomatic or asymptomatic. In our study, rate of distant metastasis in asymptomatic patients was 9.2%.

In patients with stage I and II NSCLC, a negative clinical evaluation carries a FN rate of approximately 5% [11, 13, 14]. However, in patients with clinical stage III NSCLC, the FN rate of a clinical evaluation is approximately 15% to 30% [11, 14]. It must be stressed, however, that the clinical evaluation must be carefully done, and it has been demonstrated that there should be a low threshold to investigation of subtle symptoms [15].

The primary impact of PET imaging is in distant metastasis [10, 11]. PET imaging is most useful for confirmation of the presumed preoperative extra thoracic stage in patients with intermediate stages of lung cancer. There are studies stating that the role of PET imaging is limited in patients with strong clinical signs of metastatic disease, or in patients with a clinical stage I lung cancer and a negative clinical evaluation. However, in most of these studies PET scan was used for preoperative staging.

PET scan is a reasonable alternative to a battery of other imaging studies. PET is more accurate than conventional imaging. In a study of 100 patients with lung cancer, PET imaging for distant metastases had a sensitivity of 91%, a specificity of 96%, a FP rate of 5%, and a FN rate of 7%. In contrast, conventional imaging was found to have a sensitivity of 80%, a specificity of 80%, a FP rate of 24%, and a FN rate of 17% [16]. Furthermore, PET scan is more reliable when compared specifically with a radio nucleotide bone scan. The sensitivity of PET imaging for detecting bone metastases is 90% to 92%, the specificity is 98%, the FN rate is 1% to 2%, and the FP rate is 8% to 10% [16, 17] as opposed to an average sensitivity of 76%, specificity of 69%, FP rate of 63%, and FN rate of 9% for bone scanning in patients with lung cancer [11]. Thus, the ability of PET to detect distant metastases is high, and the interpretation of a positive or negative PET result in an individual patient can be made with relative confidence. PET is also an usefull tool for the diagnosis of local recurrens [18]. However, conventional imaging of the brain is still required, because the high glucose metabolism of the brain makes PET a poor imaging test in this organ [10, 11]. In our study, PET scan was calculated to have an accuracy rate of 98%, a sensitivity of 100%, a specificity of 98%, a positive predictive value of 85% and a negative predictive value of 100% in detecting distant metastases.

As a conclusion, in the long term follow up of asymptomatic NSCLC patients, PET imaging appears to be useful as an alternative to conventional imaging to rule out unsuspected systemic disease.

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